HEMODYNAMIC MANAGEMENT OF SEPTIC SHOCK

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Clinical Spectrum of Infection

Infection

↓

Bacteremia

↓

Sepsis

↓

Severe Sepsis

↓

Septic Shock

ACCP / SCCM Consensus Definitions of SIRS and Allied Disorders

(Critical Care Med 1992 (20):864-874)

SIRS

**The systemic inflammatory response to a variety of sever
Manifested by 2 or more of the following conditions:**

Temperature	**>38 deg C or <36 deg C**
HR	**>90 beats/min**
Respiratory Rate	**>20 breaths/min or PaCO2 <32**
WBC	**>12,000 or <4,000 cells/mm3 or >10**

SEPSIS

**The systemic response to infection. Manifested by the sa
SIRS.**

ACCP / SCCM Consensus Definitions of SIRS and Allied Disorders

(Critial Care Med 1992 (20):864-874)

SEVERE SEPSIS

Sepsis associated with organ dysfunction, hypoperfusion, o
Perfusion abnormalities include but are not limited to:

lactic acidosis
oliguria
↓ mental status

SEPTIC SHOCK

Sepsis with hypotension (SBP<90), despite adequate fluid
perfusion abnormalities as listed for severe sepsis. Patien
vasopressor agents may not be hypotensive.

Incidence / Magnitude of Problem

- **300,000 to 500,000 cases of bacteremia each year in associated 20-30% mortality.**
- **200,000 bouts of septic shock.**
- **Sepsis is the leading cause of death in noncoronary i units.**
- **Mortality has changed little over the last 20 years.**
- **Incidence of sepsis appears to be increasing.**

Reasons Underlying Rising Incidence of Sepsis and Continued High Mortality

(Chest 1991 (99): 1000-09).

- **Increased patient age**
- **Increased use of cytotoxic/immunosuppresive drug therapy**
- **Increased incidence of concomittent medical illness**
- **Increased use of invasive devices for diagnosis and therapy**
- **Rising incidence of infections due to organisms other than Gram negative bacteria (Gram + bacteria, fungi, and possibly viruses)**
- **Perhabs, the emergence of antibiotic resistant organisms**

Individual Host Risk Factors

Bone, RC. The Pathogenesis of Sepsis. ***Ann Int Med*** *1991(1*

- Extremes of age
- Chronic disease
- Substance abuse
- Immunosuppressive therapy
- Vascular catheterization
- Prosthetic devices and urinary catheters
- Tracheal intubation

Brun-Bruisson et al. prospectively studied 11,828 consecutive
to 170 adult ICU's in France over a 2 month period in 1993.

Of these , 64% were medical admissions, while 18%, 14%, and
scheduled surgery, unscheduled surgery, or nonoperative traur
respectively.

They found a 9% incidence of clinically suspected and confirm
sepsis with a 28 day mortality of 56% in patients with severe s

Only 3 of 4 patients presenting with clinically suspected severe
had documented infection.

The mortality of the culture negative sepsis subgroup was stat
similar to the overall group.

JAMA. 1995 ;274: 968-974

Risk Factors for both early (<3days) and secondary (3-28 da

Simplified Acute Physiology Score (SAPS) II
# of acute organ system failures

Risk Factors for early death

low arterial pH (<7.33) (P<.001) & shock (P= .03)

Risk Factors for secondary (>3d) death

admission category (unscheduled surgery >> medical > schedule
surgery > nonoperative trauma (P<.001)

rapidly or ultimately fatal underlying disease (P<.001)

preexisting liver (P=.01) or cardiovascular (P=.02) insufficiency

hypothermia (P=.02)

thrombocytopenia (P=.01)

multiple sources of infection (P=.02)

Brun-Bruisson et al. ***JAMA, 1995, 274; 12: 968-974***

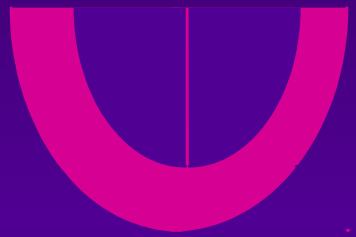
Hemodynamic Abnormalities in Septic Shock

- Prototypic example of distributive shock.
  - Severe ↓ in SVR and generalized blood flow maldistribution develop in almost all affected patients.
  - After aggresive volume loading (adequate preload), C.O. normal in 80% of patients with septic shock.
  - This is in contrast to cardiogenic, extracardiac obstructive, and hypovolemic forms of shock which ↓ C.O.
  - Initial ↓ in LVEF occuring within 24 hours of onset with associated increase in both end-systolic and end-diastolic indices.
  - This pattern of ↓ LVEF and ↑ LVEDV is characteristic of survivors and is reversible. Ventricular function/size normalize 7-10 days following onset.
  - This pattern of dysfunction was extended to the R ventricle in 1990 by Parker et al. *Chest 1990; 97:126-31.*

Changes in Cardiac Performance During Acute & Recovery Phases of Septic Shock

Parillo, JE. Pathogenetic Mechanisms of Septic Shock NEJM 328(20):1471-1477.

Acute Phase (Hypotension and Reduced SVR)



LVEDV 225 ml

LVESV 150 ml

MAP	40 mm Hg
CVP	2 mm Hg
Cardiac Output	11.25 L/min
Heart Rate	150 beats/min
SVR	270 dyn*sec*cm-5
EF	$\frac{225ml-50ml}{225ml}$ =33

Recovery Phase (Normotension)

LVEDV 125 ml

LVESV 50 ml

MAP	75 mm Hg
CVP	5 mm Hg
Cardiac Output	5.25 L/min
HR	70 beats/min
Stroke Volume	75 ml
SVR	1067 dyn*sec*cm-5
EF	$\frac{125 ml- 50 ml}{125 ml}$ =60%

Hemodynamic Patterns with Prognostic Value

- A lower heart rate at the onset of disease is predictive of survival.
- Normalization within 24 hours of either tachycardia or elevated cardiac index is associated with survival. Persistence of hyperdynamic state increases likelihood of death.
- A low ejection fraction and ventricular dilatation are also associated with survival. This perhabs reflects Frank-Starling compensation of sepsis induced myocardial depression.

Parker et al. Serial Cardiovascular Variables in Survivors and Nonsurvivors; HR as an Early Pr
Crit Care Med 1987(15): 927-9.

Parrilo, JE. Pathogenetic Mechanisms of Septic Shock, ***NEJM*** 1993; 328(20): 1471-77.

Jardin et al. (University of Vienna) prospectively studied 27
ICU patients in early septic shock.

MAP <60 mmHg.
Age range (21-76), mean 46 years old.
A-line + PAC monitoring.
11 patients (41%) had RV ejection fraction <45 %.

This group required vasoactive/inotropic drugs to achieve &
maintain an adequate perfusion pressure (MAP >60 mm H
Fluid replacement alone, (average 2850 +/- 210 ml crystall
was unsuccessful in keeping MAP >60 mmm Hg at the end
hours in these patients.

Critical Care Med 1990; 18: 1055-10

Why Is Ventricular Function Impaired ?

- High afterload due to pulmonary HTN and aggressive ventilatory support.
- Reduced preload due to fluid loss following endothelial cell injury and inappropriate vasodilation.
- Coronary perfusion may be reduced by hypotension, tachycardia and increased myocardial wall tension.
- Contractility may be impaired by circulating myocardial depressant substances, diffuse myocardial edema, and B-receptor dysfunction.

Intensive Care Med 1993; 19: 3-7.

Why Is Ventricular Function Impaired ?

- Initial hypothesis of coronary hypoperfusion leading to ischemic myocardial dysfunction was disproven by Cunnion et al., *Circulation 1986; 73: 637-44.* They showed septic patients had coronary blood flows controls, and similar myocardial lactate levels to patients with sepsis but no obvious myocardial depression.
- The presence in the bloodstream of one or more myocardial depressant substances (MDS) has been supported by in vitro myocyte preparations.

Myocardial Depressant Substance

- affect myocyte contractility in a dose dependent manner
- water soluble
- not diffuse through dialysis membrane
- moderate size molecule at least 10,000 daltons
- Purified endotoxin, IL-1, Il-2 produced no depression of myocyte contraction.
- Endotoxin and IL-2 have produced hemodynamic alterations similar to septic shock in some human studies.
- TNF, based on animal models & in vitro myocyte preparation studies appears to be one of the major mediators of cardiovascular insufficiency in septic shock.

Chest 1991; 99: 1000-09.

Role of TNF-a in Septic Shock

(Clinical Infectious Diseases 1995(20):143-58.)

- TNF-a has been proposed as the principal cytokine mediating septic-shock and sepsis related organ damage. Evidence to this effect includes:
  - High circulating TNF-a levels correlate with mortality in endotoxemia.
  - Passive immunization of some animal models with monoclonal Abs against TNF-a is protective against mortality/critical organ injury from lethal bacteremia.
  - Injection of recombinant TNF-a without LPS leads to pathophysiologic changes similar to those of bacteremia & MODS.

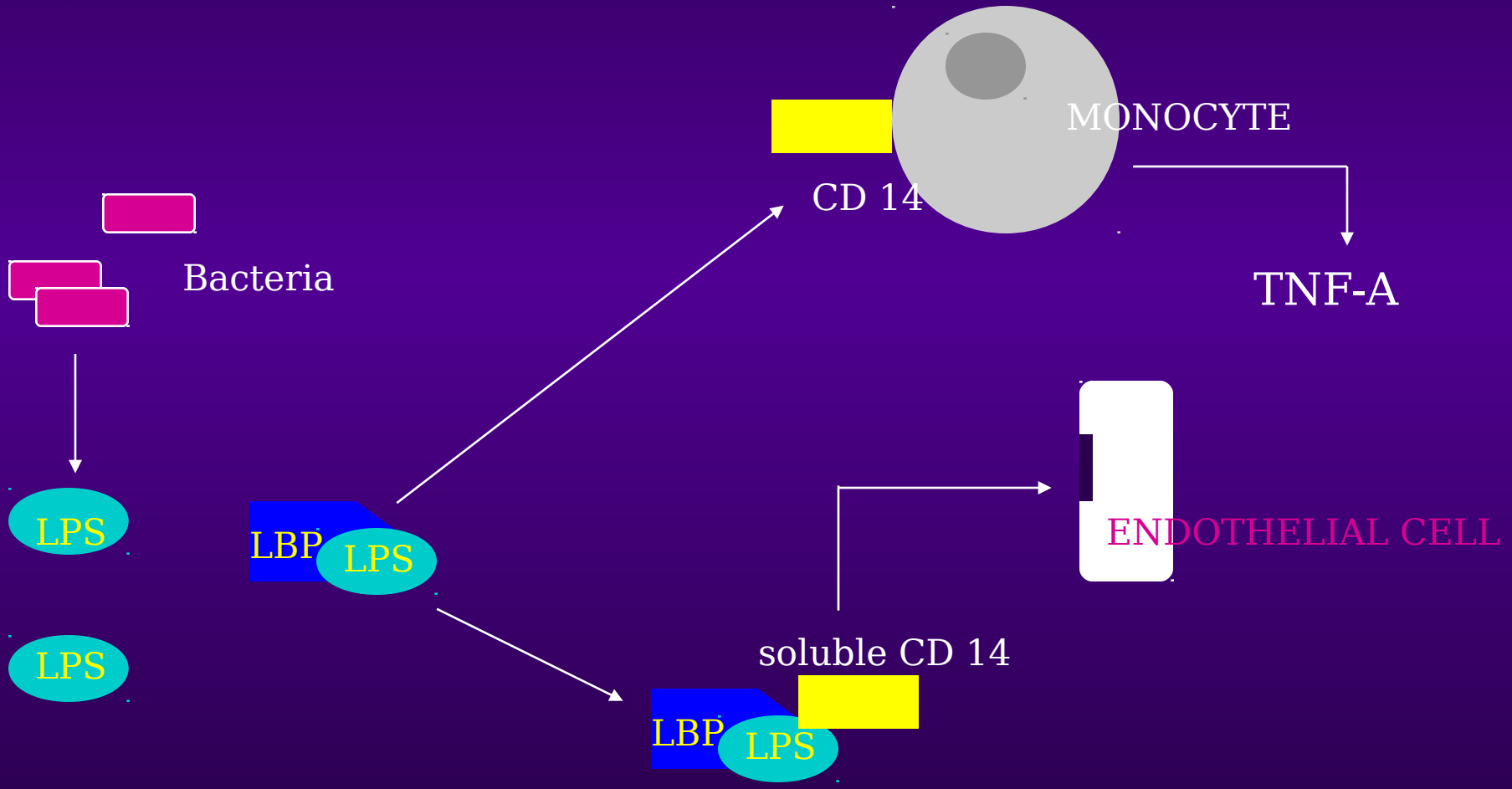
Biologic Actions of TNF-a (Cachectin)

(Hall, Schmidt, & Wood, Principles of Critical Care, McGrawHill, Inc., New Y

- Hemodynamic
  - Hyperdynamic circulatory shock
  - Capillary leak syndrome
  - Microvascular thrombosis
  - Inhibition of cardiac myocyte B-adrenergic responsiveness.
- Microbiologic
  - PMN activation, degranulation, enhanced O2 radical release.
  - Neutrophilia, lymphopenia.
  - Increased vascular permeability of the gut.
- Immunologic
  - Induction of hepatic acute phase synthesis
  - Fever
  - Promotion of IL-1, IL-2, PAF, IL-6, and eicosanoid production.
  - Stimulation of B & T lymphocyte proliferation

Pathogenesis of Septic Shock

Journal of Infection 1995; 30: 201-206.



Pathogenesis of Sepsis Mediated Hemodynamic Dysfunction

NIDUS OF INFECTION
- Pneumonia
- Peritonitis
- Cellulitis
- Abscess
- Other Infection Sites

→ ORGANISMS →

EXOGENEOUS TOXINS
- Organism
- Structural Component
- Exotoxin (TSST-1, Toxin A)
- Endotoxin

→

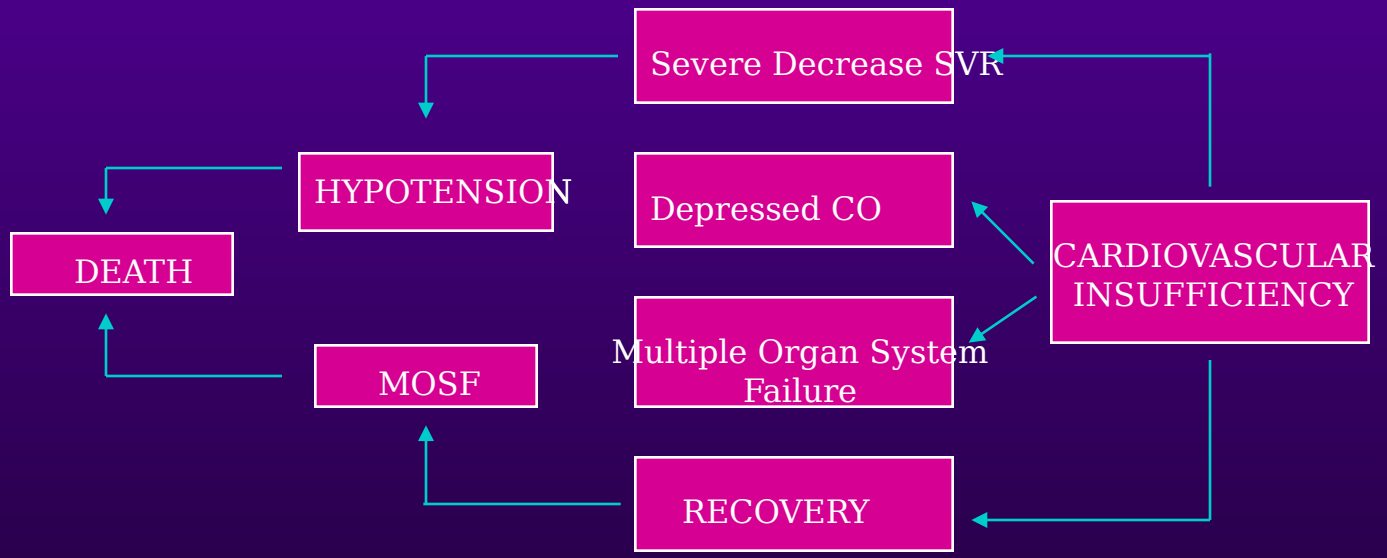
ENDOGENOUS MEDIATORS

CYTOKINES
- *Interleukin 1,2,….6
- *Tumor Necrosis Fact

PLATELET ACT FACTO

ARACHID ACID METAB

HUMORAL CASCADES
- *Complement
- *Kinins
- *Coagulation



MYOCARDIUM
- *Depression
- *Dilatation

VASCULATURE
- *Vasodilation
- *Vasoconstriction
- *Endothelial Damage
- *Maldistribution of flow

Differential Diagnosis of Septic Shock

- **Other Nonseptic Causes of Hyperdynamic Shock.**
  - overdosage of drugs with vasodilator properties
  - Toxic Shock Syndrome
  - primary/secondary adrenal insufficiency
  - anaphylactic reactions
  - severe anemia
  - severe liver disease
  - AV fistulas
  - thyroid storm
  - severe thiamine deficiency

Differential Diagnosis of Septic Shock

- The forms of shock generally associated with a vasocostricted peripheral circulation.
  - hypovolemic shock
  - cardiogenic shock
  - obstructed circulation due to embolism or tamponade

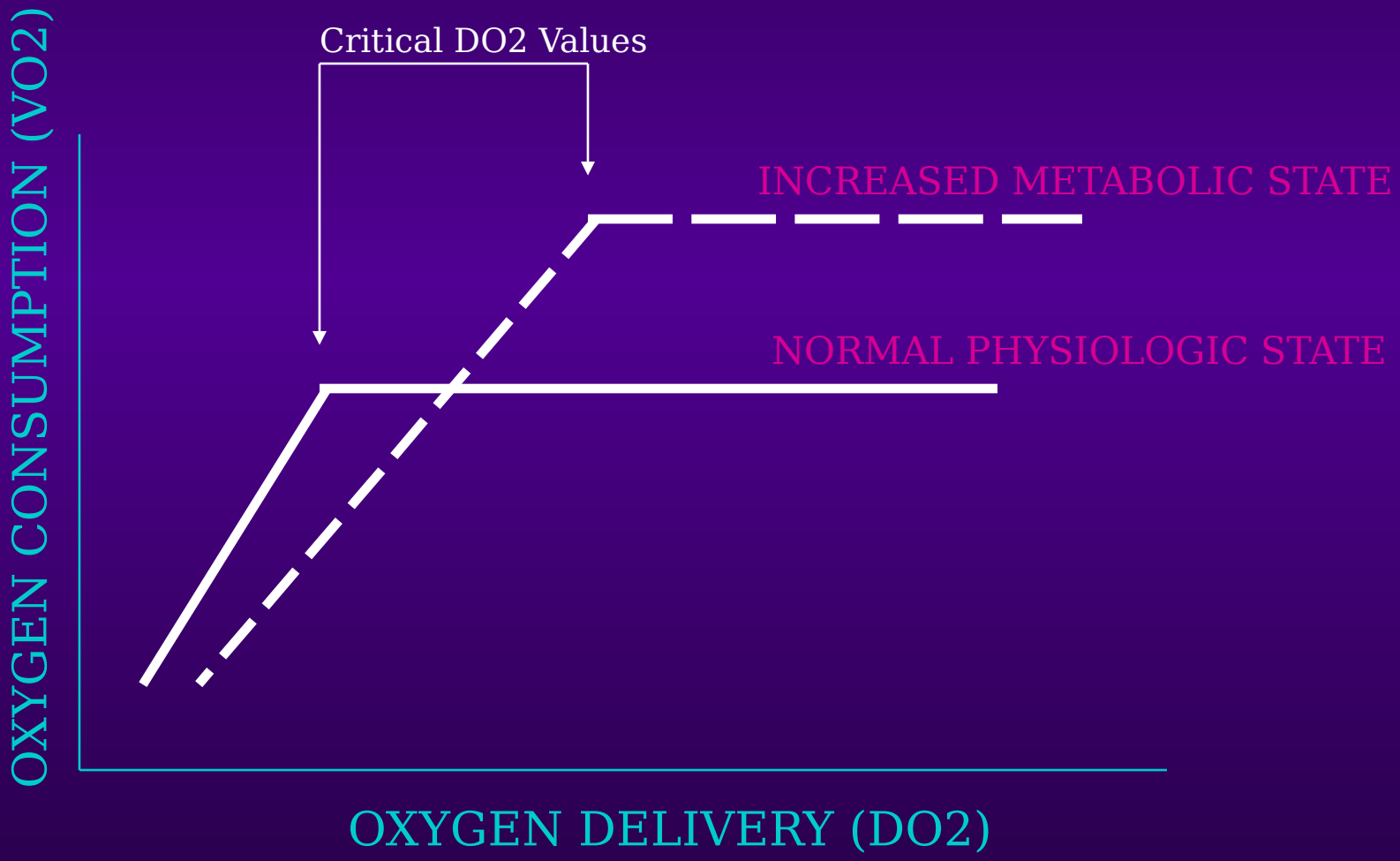
Hemodynamic Values in Sepsis Syndrome

Parameter	Normal Range	Change in Sepsis
Heart Rate	72-88 bpm	Sinus tahcycardia
MAP	70-105 mm Hg	Hypotension <60 m
CVP	2-10 cm H_2O	Normal; ↓, ↑, .
PCWP	8-12 mm Hg	Normal; ↓, ↑, .
C.O.	4-8 L/min	↑, but often not enough
C.I.	2.5-4 L/min/m2	to compensate for ↓
SVR	770-1550 dyne/sec/cm5	<600 if no pressors
SVRI	1760-2600 dyne/sec/cm5/m2	<1000 if no pressor
DO2	520-720 mL/min/m2	Normal; may be ↓ due to h or shunting
VO2	100-180 mL/min/m2	Typically ↑.

Oxygen Delivery

- CaO_2 = 1.34(gm Hgb/dL)(SpO_2) + 0.0031(PaO_2)
- DO_2 = C.O. x CaO_2
- VO_2 = C.O. x (CaO_2 - CvO_2)
- O_2ER = (CaO_2 - CvO_2)/ CaO_2
- Normal range of O_2ER is 0.2 to 0.3
- Critical DO_2 in patients undergoing elective CPB was 330 ml/kg/m2
- Critical DO_2 and critical O_2ER determined during withdrawal of therapy in critically ill dying patients were 4.5 and 0.6 ml/kg/min.
  - Arterial lactate levels increase progressively as O2 delivery decreases below these critical values.

SUPPLY DEPENDENT O2 CONSUMPTION



In the 1980's Shoemaker championed the concept that normalizing hemodynamic parameters in hyperdyna surgical patients was not good enough. His observationa of 708 high risk surgical patients without cardiovascular disease showed that post-op increases in CI, DO2, and V values were greater in survivors than in non-survivors.

Maximum cumulative VO2 deficit averaged

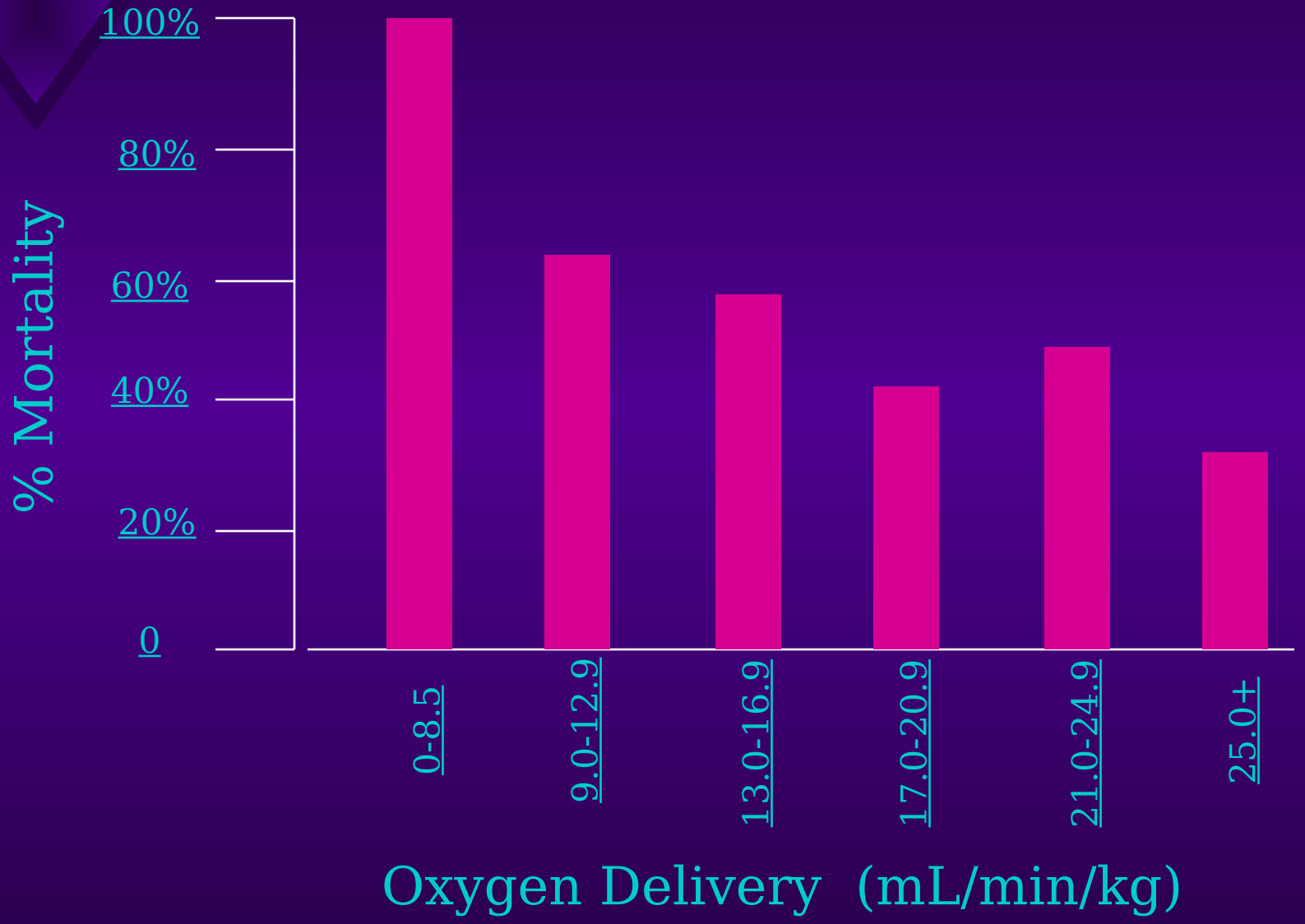
- 33.5 in nonsurvivors
- 26.8 in survivors with organ failure
- 8.0 in survivors without organ failure

Nonsurvivors took longer to reach their maximum cumul VO2 deficit, and the duration of the deficit was greater.

He argued that since increased VO2 requirements can o reduced slowly via medical intervention in patients with shock, increasing DO2 is the most plausible strategy for tissue oxygen debt.

Shoemaker WC, Appell PL, Kram HB, Waxman R, Lee T-S. Prospective trial of supranormal values of survivors as theraputic goals in high risk surgical p 1988; 94: 1176-86.

Tuchsmidt J, Fried J, Astiz M, Rackow E. Elevation of cardiac oxygen delivery improves outcome in septic shock. *Chest* 1992; 102: 216-220.



Therapeutic Goals

- For Postoperative Patients
  - C.I. 50 % > normal
  - Blood volume 500 ml > normal if PCWP < 20 mm Hg.
  - DO2 > 600 ml/min/m2
  - VO2 > 170 ml/min/m2
- For septic patients
  - C.I. 50-100% > normal
  - Blood volume 500 ml > normal if PCWP < 20 mm Hg.
  - DO2 > 800-1000 ml/min/m2
  - VO2 > 180 ml/min/m2

Most investigators currently agree that increa
DO2 is associated with survival.

Does increasing DO2 in the critically ill patien
improve survival or is it a marker for the heal
patient who is more likely to survive ?

Evidence for Maintenance of Supranormal Levels of DO_2 in the Critically Ill

- Acute endotoxemia and acute bacteremia animal models of sepsis induce a pathologic dependence of VO2 on DO2.
- Numerous clinical studies of ARDS, sepsis syndrome, septic shock, and critical illness claim to show pathologic dependence of VO2 on DO2.
- Several clinical studies have found that survivors of critical illness have greater DO2 and VO2 than nonsurvivors.
- Some clinical studies claim to show that nonsurvivors of critical illness have pathologic dependence of VO2 on DO2, while survivors do not, suggesting nonsurvivors have an occult oxygen debt.
- Several randomized control studies of increased vs normal DO2 found decreased mortality in patients who received increased DO2.

Am J Resp Crit Care Med 1994; 149: 533-537.

Evidence Against Maintenance of Supranormal DO_2

- Studies reporting pathologic supply-demand O2 consumption should be interpreted with caution:
  - VO_2 and DO_2 are both calculated values sharing C.O. and CaO_2
  - Archie et al., 1981, showed that randomly generated numbers in a mathematicaly coupled relationship can result in significant correlation which is entirely artifactual. *Ann Surg 1981; 193: 296-303.*
- In every study of ARDS and/or sepsis in which VO_2 & DO_2 were measured independently, VO_2 was not dependent on DO_2. In several studies, calculated VO_2 was found to be dependent on DO_2, but measured VO_2 was not.

Calculated VO2		Dependence		Measured VO2		Depe
ARDS						
Powers	(73)		Y	Lutch	(72)	N
Donek	(80)	Y		Annat	(86)	N
Bihari	(87)	Y		Cartile	(89)	N
Fenwick	(90)		Y	Ronco	(91)	N
SEPSIS						
Kaufman	(84)		Y	Vermeij	(90)	
Haupt	(85)	Y		Ronco	(93)	N
Gilbert	(86)	Y				
Vincent	(90)		Y			

Am J Resp Crit Care Med 1994; 149: 533-537.

Evidence Against Maintenance of Supranormal DO_2

- The "apparent" relationship between O2 delivery & consumption may represent normal physiology; increases in DO2 occur in response to spontaneous changes in VO2. This can be misinterpreted as supply-dependent O2 consumption.

- The "normal" critical O2 delivery value & the O2ER have been derived in animal studies but not in humans. Attempts to identify these points in anesthetized cardiac surgical and critically ill patients used regression analysis of pooled data from multiple patients rather than individual patients.

Vasoactive Agent Receptor Activity

Agent	a1	a2	b1	b2	Dopa
Dobutamine	+	+	++++	++	0
Dopamine	++/+++	?	++++	++	+
Epinephrine	++++	++++	++++	+++	
Norepinephrine	+++	+++	+/++	0	
Phenylephrine	++/+++	+	?	0	

Cardiac Receptors

- Mainly contains B1 receptors ↑ >>> chronotropy, inotropy, dromotropy.
- B2 stimulation >>> ↑ rate, inotropy due to activation of adenylate cyclase and ↑ cAMP
- Postsynaptic a1 receptors have recently been described in the human heart.
  - ↑ contractility
  - do not ↑ rate.
- Presynaptic a2 receptors are activated by Ne released by the sympathetic nerve, inhibiting further release.

Dopamine

- Recommended as the initial drug of choice by many clinicians it increases both myocardial contractility and SVR via *a* and *B* receptors.
- May help maintain splanchnic circulation, urine output and renal function via dopa receptor action.
  - 1-3 mcg/kg/min- *dopa* receptors
  - 3-10 mcg/kg/min *B* receptors
  - >10 mcg/kg/min *a* receptors
- Increases heart rate
- Can cause tachyarrythmias
- May also increase Pcwp via pulmonary artery vasoconstriction.

Dobutamine

- Ruffolo et al. showed that the B1 and B2 activity of dobutamine resides in the (+) isomer and the (-) isomer directly stimulates A1 receptors in the heart.
- Dobutamine produces a larger increase in cardiac output and is less arrythmogenic than dopamine.
  - The strong inotropic action of dobutamine is a function of the additive effects of its A1 and B1 activity, and the weak chronotropic effect of the (+) isomer on the B receptors. *Crit Care Med 96;24(3):525-537.*
- The B2 vasodilatory effect of dobutamine often require its use as an adjunct to other catecholamines with more predominant A or B1 effects.
- Tolerance to the inotropic effects of dobutamine has been demonstrated after 72 hrs in CHF patients. *Am J Med 1980; 69: 262-266.*

Dobutamine vs Dopamine

- Vincent et al., 1987, compared dobutamine with dopamine @ 6 mcg/kg/minin 24 dogs with endotoxin mediated septic shock.
  - Per given amount of saline infused, dopamine resulted in higher cardiac filling pressures, whereas dobutamine resulted in higher cardiac output.
  - When fluid infusion was titrated to maintain Pcwp constant,significantly more fluid (109 vs 71 ml/kg) was required with dobutamine.
  - The dobutamine group had greater SV (39.6 vs 21 ml) and VO2 (194 vs 144 ml/min). *Anesth & Analg 87; 66:565-71.*
- Several studies done in patients with cardiogenic shock, severe CHF,& respiratory failure reported similar findings.

Does Dobutamine Improve Cerebral VO_2 and Septic Encephalopathy?

- Berre et al., studied 14 mechanically ventilated septic patients with altered mental status and stable hemodynamic status.
  - They measured mean flow velocity in the right MCA by TCD while incrementally infusing dobutamine 2-10 mcg/kg/min.
  - Cerebral A-V O_2 content difference and cerebral O_2ER ↑ while mean flow velocity in the R MCA ↑ from 68 to 80 cm/sec.
  - Cerebral DO_2 ↑ by 12% with dobutamine use while cerebral VO_2 did not change. *Crit Care Med 97; 25(3): 392-398.*
- This and several animal studies suggest that ↑ DO_2 does not appear to be of benefit in septic encephalopathy.

Phenylephrine

- a-1 agonist. Increases SVR & BP.
- May also increase contractility & thus C.O.
- Yamazaki (1982) evaluated 7 hyperdynamic & hypotensive patients against 8 controls with heart disease.
  - He used an infusion of 70 mcg/min to SBP by 30 mm Hg.
  - In septic patients, CI, SI, BP, CVP & HR all .
  - In the cardiac group , BP, HR, & SVR but CI & SI .
- Dasta (1993) treated 7 nonhypotensive but hyperdynamic SICU patients with doses of phenylephrine (0.5 8 mcg/kg/min range) over 3 hours. DO2 and hemodynamics by 15%, VO2 in all but 1 patient.

Phenylephrine

- Gregory et al., treated 13 SICU patients with septic shock with phenylephrine (0.5-9 mcg/kg/min) in combination with dopamine / dobutamine.
  - VO2 ↑ from 145 ml/min/m2 baseline to 200 ml/min/m2. ↑ Lactate ↓ urine output , & SCR remained unchanged.
  - MAP, SVRI, SVI, & LVSWI all ↑ . PCWP & HR were unchanged. *Crit Care Med 1991; 19: 1395-1400.*
- Phenylephrine, alone or in combination with dobutamine or dopamine, ↑ cardiac index, MAP, SVI, DO2 and VO2. Lactate ↓ .

Norepinephrine

- First used 3 decades ago for the treatment of hypotensive states before development of the synthetic catecholamines dopamine & dobutamine.
- Most of the studies evaluating norepinephrine used it after failure of dopamine or dopamine/dobutamine to improve hemodynamic status.
- All of the studies found a significant ↑ in MAP with either a ↓ or no change in HR.
- CI either ↑ or did not change, and Pcwp did not change.
- Seven studies evaluated urine output.
  - Four found an increase
  - One found no change
  - Two found a variable effect
  - No study showed a ↓ in urine output or a predisposition to ARF.

Martin et al., directly compared NE with dopamine in a prospecti
blind, randomized study of 32 hyperdynamic septic shock patient
fluid administration.

Patients received either DOPA (2.5-25 mcg/kg/min) or NE (0.5-
5 mcg/min) with the goals of:

SVRI > 1100 dynes/m2/cm5
MAP > 80 mm Hg
CI > 4 L/min/m2
DO2 > 550 ml/min/m2
VO2 > 150 mL/min/m2

Dopamine administration achieved these goals in only 5/16 patie
15/16 (93%) with NE.

10 of 11 patients who did not respond initially to DOPA responde

No deleterious effect of NE on urine output noted, but study only

Chest 1993; 103: 1826-31.

Epinephrine

- Traditionally used when dopamine/dobutamine failed.
- Miran et al., prospectively studied 18 patients with septic shock, mean age 64, in an university ICU. In doses of 3-18 mcg/min, EPI ↑ HR, MAP, CI, LVSWI, SVI, VO2, and DO2. Pcwp, mean PAP, and SVRI were unchanged. *Crit Care Med 93; 21(1): 70-77.*
- McKenzie et al., treated 13 volume replete septic patients with doses of 0.005 - 0.42 (mean 0.16) mcg/kg/min to C.I. > 4.5, and DO2 > 600 ml/min/m2. MAP, CI, LVSWI, and DO2 ↑. SVR, VO2 were unchanged, and O2ER ↓. 54% of the patients died.
  Intensive Care Med 91; 17:36-39.
- In 14 patients unresponsive to fluid, dopamine, and dobutamine, with PAC diagnosed RV dysfunction, epinephrine (0.1 to 1 mcg/kg/min) improved RV contractility. MAP, CI, SVI all ↑. Pcwp, SVR, & HR were unchanged. Overall mortality 64%.

Intensive Care Med 97; 23: 664-670.

In a crossover study of 8 septic patients using 2 hour infusi
epinephrine versus norepinephrine +dobutamine during ma
of stable temperature and stable Pcwp using HES, splanchn
flow was 43% lower with epinephrine, and splanchinc VO2
lower ↓(splanchnic O2ER).

Effects on global hemodynamic and O2 transport variables
HR, MAP, Pcwp, CI, SVR, and global DO2 and VO2 were sim

Splanchnic perfusion was evaluated using hepatic vein cath
under fluoroscopy and indocyanine green dye dilution.

Meier-Hellman et al.,Crit Care Med 97; 25(3): 399-404

Levy et al., found that the addition of dobutamine 5 mcg/kg
epinephrine infusion in 20 septic patients had no significant
on HR, MAP, CI, SVR, DO2, and VO2 but improved gastric m
perfusion based on gastric intramucosal pCO2 and pH meas

Crit Care Med 97; 25(10); 1649-53.

Amrinone ???

- Phosphodiesterase III inhibitor; increases intracellular cAMP levels.
- Increases LV contractility in patients with severe CHF and dilated cardiomyopathy.
- Vasodilation and afterload reduction.
- ↑ speed of relaxation of the left ventricle & may therefore affect diastolic filling.
- Werner et al., 1995, studied amrinone in 6 pigs treated with endotoxin and 7 nonendotoxemic pigs (all anesthetized with ketamine, isoflurane, and pancuronium.
  - Amrinone ↓ the reduced diastolic compliance seen in endotoxemia
  - Amrinone ↑ LV contractility in septic pigs to a much greater extent than in the control group.
  - Amrinone further ↓ MAP by 10% above the 34% ↓ in septic pigs.

    Am J Resp Crit Care Med 1995;152: 496-503.

Perfusion Goals in Patients with Septic Shock

HEMODYNAMCS

PCWP >10 but <20 mm Hg
MAP > 60 mm Hg
CI > 3 L/min/m2

ORGAN PERFUSION

CNS - improved sensorium
Skin - warm, well perfused
Renal - UOP > 1 cc/kg/hr

O2 DELIVERY ADEQUACY

Arterial Hgb SpO2 > 95%
Hgb concentration > 10 gm/dL
SVO2 > 30 mm Hg
Blood Lactate Conc < 2 mM/L

Initial Resuscitation of Septic Shock

1. Secure airway if respirations ineffective or patient unable to protect his airway.
   - Patients with hypotension not responding promptly to acute volume expansion should also be intubated to prevent respiratory arrest.
   - Supplemental O2
2. Fluid resuscitation- follow BP, respiration, pulse, UOP, mental status, and CVP to assess response.
3. If circulatory status fails to improve after 2-3 L or signs of fluid overload develop consider vasoactive agents.
4. Consider placing a PAC as this will allow better titration of hemodynamic drugs and assessment of circulatory status.

Resuscitation (cont.)

- Both Shoemaker & Hall recommend starting initially with dopamine in low doses (2-5 mcg/kg/min) as this will not only improve perfusion pressure but may help preserve renal function.
- The dose can then be titrated upward or NE added to achieve and maintain a MAP of at least 60 mm Hg.
- Blood cultures and initial laboratory values which assess end organ function should be sent off- CBC, P1, P2, P3, PT/PTT, UA.
- Early institution of appropriate antibiotic therapy is crucial. Delay in initiating antibiotics or initiation of antibiotic therapy which does not cover the offending agent are associated with a worse outcome.
- This initial resuscitation should ideally be accomplished within 1 hour.

THE END